

thereof, said second DNA segment comprises an *attP* sequence according to SEQ ID NO:2 or a derivative thereof, wherein if said first DNA segment comprises an *attP* sequence according to SEQ ID NO:2 or a derivative thereof, said second DNA segment comprises an *attB* sequence according to SEQ ID NO:1 or a derivative thereof, wherein if said first DNA segment comprises an *attL* sequence according to SEQ ID NO:3 or a derivative thereof said second DNA segment comprises an *attR* sequence according to SEQ ID NO:4 or a derivative thereof, or wherein if said first DNA segment comprises an *attR* sequence according to SEQ ID NO:4 or a derivative thereof said second DNA segment comprises an *attL* sequence according to SEQ ID NO:3 or a derivative thereof; and

wherein said cell further expresses a bacteriophage *lambda* integrase Int, which induces sequence specific recombination through said *attB* and *attP* or *attR* and *attL* sequences.

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- 30. (New) The method of claim 29, wherein said first DNA segment was introduced into the genome of said cell by recombinant methods.
- 31. (New) The method of claim 29, wherein said first DNA segment is naturally-occurring in the genome of said cell.
- 32. (New) The method of claim 29, wherein said first DNA segment comprises an *attB* sequence according to SEQ ID NO:1 or a derivative thereof, and said second DNA comprises an *attP* sequence according to SEQ ID NO:2 or a derivative thereof.
- 33. (New) The method of claim 29, wherein said first DNA segment comprises an *attP* sequence according to SEQ ID NO:2 or a derivative thereof, and said second DNA comprises an *attB* sequence according to SEQ ID NO:1 or a derivative thereof.
- 34. (New) The method of claim 29, wherein said first DNA segment comprises an *attL* sequence according to SEQ ID NO:3 or a derivative thereof, and said second DNA sequence comprises an *attR* sequence according to SEQ ID NO:4 or a derivative thereof, further comprising, in step (c), providing to said cell a Xis factor.

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- 35. (New) The method of claim 29, wherein said first DNA segment comprises an *attR* sequence according to SEQ ID NO:4 or a derivative thereof, and said second DNA sequence comprises an *attL* sequence according to SEQ ID NO:3 or a derivative thereof, further comprising, in step (c), providing to said cell a *Xis* factor.
- 36. (New) The method of claim 29, further comprising providing to said cell a third DNA segment comprising an *Int* gene. ((Steve, the third segment should only be the *Int* gene, the fourth segment should be the *Xis* factor gene. The *Int* is essential for the recombination of all four *att*-sites, the *Xis* factor gene only for the reaction between *attR* and *attL*.))
- 37. (New) The method of claim 36, further comprising providing to said cell a fourth DNA segment comprising *Xis* factor gene, respectively.
- 38. (New) The method of claim 36, wherein said third DNA segment further comprises a regulatory sequence effecting a spatial and/or temporal expression of the *Int* gene. ((Steve, please take care that all possibilities of original claim 6 are claimed))
- 39. (New) The method of claim 37, wherein said fourth DNA segment further comprises a regulatory sequence effecting a spatial and/or temporal expression fo the *Xis* factor gene.
- 40. (New) The method of claim 29 wherein said *Int* is a modified integrase.
- 41. (New) The method of claim 37, wherein said modified *Int* is *Int-h* or *Int-h/218*.
- 42. (New) The method according to claim 29, wherein in step (c) further comprises providing an "integration host factor" (IHF).
- 43. (New) The method according to claim 29, wherein said first and/or second DNA segment further comprise a sequence effecting integration of said first and/or second DNA segment into the genome of said cell by homologous recombination.
- 44. (New) The method of claim 29, wherein said first and/or second DNA segment further comprises a sequence coding for a polypeptide of interest.

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- 45. (New) The method of claim 44, wherein said polypeptide of interest is a structural protein, an endogenous or exogenous enzyme, a regulatory protein or a marker protein.
- 46. (New) The method of claim 29, wherein said first and second DNA segment are introduced into the eukaryotic cell on the same DNA molecule.
- 47. (New) The method of claim 29, wherein said eukaryotic cell is a mammalian cell.
- 48. (New) The method of claim 47, wherein said mammalian cell is a human, simian, mouse, rat, rabbit, hamster, goat, bovine, sheep or pig cell.
- 49. (New) The method of claim 29, further comprising:
 - (d) performing a second sequence specific recombination of DNA by an Int and a Xis factor after the steps (a)-(c), wherein said first DNA sequence comprises said *attB* sequence according to SEQ ID NO:1 or a derivative thereof and said second DNA sequence comprises the *attP* sequence according to SEQ ID NO:2 or a derivative thereof, or wherein said first DNA sequence comprises said *attP* sequence according to SEQ ID NO:2 or a derivative thereof and said second DNA sequence comprises the *attB* sequence according to SEQ ID NO:1 or a derivative thereof.
- 50. (New) The method of claim 49, further introducing a further DNA sequence into said cells, the further DNA sequence comprising a Xis factor gene.
- 51. (New) The method of claim 50, wherein said further DNA sequence comprises further a regulatory DNA sequence effecting a spatial and/or temporal expression of said Xis factor gene.
- 52. (New) The method of claim 29, wherein said method is performed in a vertebrate organism.
- 53. (New) The method of claim 52, wherein said vertebrate organism is a human.

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- 54. (New) A nucleic acid comprising the sequence of SEQ ID NO:5, or a derivative thereof having as many as six substitutions, with the provision that the derivative is not the wild-type *attP* sequence.
- 55. (New) A vector comprising:
 - (a) a nucleic acid segment comprising the sequence of SEQ ID NO:5, or a derivative thereof having as many as six substitutions, with the provision that the derivative is not the wild-type *attP* sequence; and
 - (b) a nucleic acid segment coding for a selected gene or a fragment thereof.
- 56. (New) The vector of claim 53, wherein said selected gene is the CFTR gene, ADA gene, LDL receptor gene, β globin gene, Factor VIII gene or Factor IX gene, alpha-1-antitrypsin gene or the dystropin gene or a gene fragment of one of said genes.
- 57. (New) The vector of 53, further comprising a nucleic acid segment comprising a regulatory element.
- 58. (New) A eukaryotic cell obtainable according to the method of claim 29.
- 59. (New) A non-human transgenic organism comprising at least one cell made according to the method of claim 29.
- 60. (New) The organism according to claim 54, wherein said organism is a mouse, rat rabbit or hamster.

REMARKS

Should the examiner have any questions regarding the content of this preliminary amendment, a telephone call to the undersigned is invited.